The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 16

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte SHERVIN K. PISHEVAR

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Appeal No. 2000-1919
Application No. 08/831,993

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ON BRIEF

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Before ROBINSON, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2, 4-12, and 14-20, all of the claims remaining. Claim 1 is representative and reads as follows:

1. A method for inhibiting the development of a parasite in a erythrocyte, said method comprising the step of contacting the erythrocyte, infected with an intracellular parasite, with a magainin, PGLa or XPF peptide under conditions whereby the development of said parasite in said erythrocyte is inhibited.

The examiner relies on the following references:

Pasvol et al. (Pasvol), "Separation of viable schizont-infected red cells of Plasmodium falciparum from human blood," Annals of Tropical Medicine and Parasitology, Vol. 72, No. 1, pp. 87-88 (1978)

Gwadz et al. (Gwadz), "Effects of Magainins and Cecropins on the Sporogonic Development of Malaria Parasites in Mosquitoes," Infection and Immunity, Vol. 57, No. 9, pp. 2628-2633 (1989)

Cabantchik, "Properties of Permeation Pathways Induced in the Human Red Cell Membrane by Malaria Parasites," Blood Cells, Vol. 16, pp. 421-432 (1990)

Magowan et al. (Magowan), "Role of the Plasmodium falciparum Mature-Parasite-Infected Erythrocyte Surface Antigen (MESA/PfEMP-2) in Malarial Infection of Erythrocytes," Blood, Vol. 86, No. 8, pp. 3196-3204 (1995)

Matsuzaki et al. (Matsuzaki 1), "Molecular Basis for Membrane Selectivity of an Antimicrobial Peptide, Magainin 2," Biochemistry, Vol. 34, pp. 3423-3429 (1995)

Matsuzaki et al. (Matsuzaki 2), "Translocation of a Channel-Forming Antimicrobial Peptide, Magainin 2, across Lipid Bilayers by Forming a Pore," Biochemistry, Vol. 34, pp. 6521-6526 (1995)

Matsuzaki et al. (Matsuzaki 3), "Kinetics of Pore Formation by an Antimicrobial Peptide, Magainin 2, in Phospholipid Bilayers," Biochemistry, Vol. 34, pp. 12553-12559 (1995)

Claims 1, 2, 4-12, and 14-20 stand rejected under 35 U.S.C. § 112, first paragraph, as unsupported by an enabling disclosure.

We reverse.

Background

"Magainins, PGLa and XPF comprise a class of linear, amphipathic cationic peptides originally found in the skin of Xenopus laevis and shown to have broad-spectrum antimicrobial activity. . . . [M]againins have been reported to disrupt extracellular stages of Plasmodia parasites. Unfortunately, the life cycles of the Plasmodia, like many intracellular pathogens, comprise only brief

extracellular stages and the magainins were reported to have no effect on their intracellular development." Specification, page 1.

The specification discloses "methods and compositions for inhibiting the development of intracellular parasites by treating [infected] cells with an effective concentration of a magainin, PGLa or XPF peptide under conditions whereby the development of the parasite in said cell is inhibited. The targeted parasites have been found to increase in [sic] the accessibility of the plasma membrane of the cell to the peptide and effect an increase in the cytopathic, especially lytic, sensitivity of the cell to the peptide." Page 2.

The specification provides two working examples. In the first example, human red blood cells infected with Plasmodium falciparum parasites were treated with increasing doses of a magainin peptide ("magainin 2") and parasitemia was assayed daily for four days. The results showed >50% reduction in parasitemia in the highest-dosage sample as compared to the untreated control cells by the fourth day. See Table 1 (page 5). Appellant concluded that "[t]he data demonstrate dose and time dependent inhibitions of parasitemia by the magainin peptide." Page 6.

The second example discloses an immunofluorescent assay to determine the location of the magainin peptide within treated erythrocytes. Plasmodium-infected cells treated with magainin 2 as in the first example were assayed using an antibody against magainin 2 at different times and different magainin concentrations. Appellant found that "[a]t each time point at each magainin

concentration, the antibody was visualized exclusively within the parasite inside infected erythrocytes." Page 6.

Discussion

The examiner rejected all of the claims as nonenabled because the claimed effect on intracellular parasites is contrary to what would be expected based on the prior art. See the Examiner's Answer, pages 3-4 (emphasis in original):

> Gwadz et al. teach that the magainin peptide could disrupt extracellular stages of the parasites but had no effect on intracellular development. . . . [T]he question is whether there is a predictability in the prior art that, despite the cited teaching of Gwadz et al., magainins can [a]ffect intracellular development of malaria parasites. . . . The prior art, however, does not indicate that magainins, instead of being either bound to plasma membrane of a cell or lysing a cell altogether, are capable of permeating into intracellular space of a live cell.
>
> The instant disclosure provides no evidence that the observed effects of magainin on malaria parasites are due to inhibition of parasite's intracellular development, and is [sic] not due to effect of magainins on parasites located outside erythrocytes (the latter effect is well documented in prior art).

The examiner acknowledges the working examples in the specification but disputes their probative value. The examiner characterized the first example as providing "[n]o evidence" to support the claimed invention. See the Examiner's Answer, pages 4-5:

> Example 1 offers Table 1 with some unidentifiable numbers and informs that parasitemia assays were performed according to Pasvol or Magovan. The cited references, however, teach a number of assays and various ways of data analysis which make it impossible to one skilled in art to identify the origin of the numbers presented in the instant Table 1. Further, because the description of Example 1 informs that magainin was added in extracellular

> medium, the numbers presented in the Table may equally reflect extracellular effect of the peptide on the parasite (i.e. described in the prior art), or inhibition of intracellular development of the parasite (i.e. asserted in the application). No evidence for the latter is provided.

The examiner was also unimpressed by the second working example. See the Examiner's Answer, page 5:

> Turning to Example 2, the uniformly overexposed image of a cell stained with antibody against magainin 2 . . .reflect[s] one of three possibilities: 1) stained magainin is located outside the cell; 2) stained magainin is bound to the plasma membrane (as suggested by the prior art, see above), or 3) stained magainin is located inside a cell. Again, no evidence for the latter is offered.

The examiner cited an additional basis of non-enablement for claims 1 and 11. These claims read on using any of three classes of peptides—magainins, PGLa or XPF peptides—in the claimed method, but the working examples in the specification are limited to magainins. The examiner concluded that the specification does not enable the full scope of these claims because it "does not provide guidance on how to use PGLa or XPF peptide, how to select effective concentration for PGLa vs XPF peptide vs magainin. Therefore, insufficient guidance exist[s] in the specification to enable a person of ordinary skill in the art to practice the invention without the need for undue experimentation." Examiner's Answer, page 5.

Appellant argues that "[t]he application provides all the teaching necessary for one skilled in the art to practice the invention without undue experimentation." Revised Appeal Brief, page 3. In support, Appellant has submitted a declaration under 37 CFR § 1.132 by Steve Ludtke. Dr. Ludtke states that, in his opinion,

"the application teaches in detail everything one of ordinary skill in the art needs to practice the invention (i.e. inhibit the development of intracellular parasites in erythrocytes) without the need for any experimentation beyond routine screening in simple, disclosed assays." Ludtke declaration, paragraph 2.

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." In re Marzocchi, 58 CCPA 1069, 1073, 439 F.2d 220, 224, 169 USPQ 367, 370 (1971).

In this case, the weight of the evidence in the record supports Appellant's position rather than the examiner's. The examiner cited Gwadz and two papers by Matsuzaki as "indicat[ing] that magainins do not have effect on the intracellular parasite as they do not penetrate inside the cells." Examiner's

Answer, page 6 (emphasis in original). We have reviewed the cited references, however, and we do not find that they provide evidence to support the examiner's conclusion. Gwadz states that "[i]n vitro studies . . . showed that the magainin peptide could disrupt extracellular stages of [plasmodial] parasites but that it had no effect on intracellular development." Page 2628, right-hand column. However, Gwadz provides no evidence to support this conclusion, citing only "unpublished data." Id.

The Matsuzaki references cited by the examiner also do not support his position. Matsuzaki investigated the molecular basis of the effect of magainins on different membranes and the translocation of magainin peptides from one side of a membrane to the other. The examiner has not adequately explained how either Matsuzaki reference contradicts the data in the instant specification or shows that magainins do not penetrate inside cells.

Appellant's position, on the other hand, is supported by the working examples in the specification. The examiner has complained that the presentation of the data in the specification makes it difficult for him to independently evaluate whether they support the specification's conclusions. However, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

Marzocchi, 439 F.2d at 223, 169 USPQ at 369, emphasis in original. The examiner's complaints about the data in this case do not provide a sufficient basis "to doubt the objective truth of the statements" in the specification.

Appellant's position is also supported by the Ludtke declaration. Dr. Ludtke declares that "the application teaches in detail everything one of ordinary skill in the art needs to practice the invention (i.e. inhibit the development of intracellular parasites in erythrocytes) without the need for any experimentation beyond routine screening." Ludtke declaration, paragraph 2. The examiner has cited no evidence that contradicts the Ludtke declaration. Rather, he dismissed it as "not provid[ing] any further factual evidence and merely cit[ing] the specification." Examiner's Answer, page 8. Therefore, as Appellant notes, the Ludtke declaration remains uncontroverted as evidence that the claims are fully enabled by the specification. Reply Brief, page 1.

With respect to the PGLa and XPF peptides encompassed by claims 1 and 11, Appellant argues that "[t]he use of PGLa and XPF peptides is the same as the structurally analogous magainin peptides. . . . Substituting one taught peptide for another taught peptide does not require undue experimentation." Revised Appeal Brief, page 4. The examiner provided no substantive response (see the Examiner's Answer, page 8) and no evidence or reasoning on which to base a conclusion that using PGLa or XPF peptides in the claimed method would require undue experimentation. We therefore conclude that the examiner has not met his burden of showing nonenablement with respect to this limitation.

We conclude that the examiner has not met his burden of "setting forth a reasonable explanation," Wright, 999 F.2d at 1561-62, 27 USPQ2d at 1513, as to why he doubts the accuracy of the specification's assertions. Even if it is true that Appellant's data could be better explained, or the photographic data could be better reproduced, the examiner must do more than simply state that he cannot interpret the data. The examiner's burden is to "explain why [he] doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of [his] own with acceptable evidence or reasoning which is inconsistent with the contested statement." Marzocchi, 439 F.2d at 224, 169 USPQ at 370. This burden has not been carried here. Therefore, the examiner has not made out a prima facie case of non-enablement.

Summary

We reverse the rejection for non-enablement because the weight of the evidence of record supports Appellant's position rather than the examiner's.

REVERSED

DOUGLAS W. ROBINSON Administrative Patent Judge	)
DEMETRA J. MILLS Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
ERIC GRIMES Administrative Patent Judge	)

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